

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Applicants: Lars KARLSSON, Wai-Ping LEUNG, Per A. PETERSON and  
Christopher ALFONSO

Serial No.: Not Assigned

Art Unit: 1632

Filed: 28 February 2002

Examiner: BAKER, A.

For: H2-O MODIFIED TRANSGENIC ANIMALS

Assistant Commissioner for Patents

Box: PATENT APPLICATION

Washington, D.C. 20231

**PRELIMINARY AMENDMENT**

Sir:

Applicants respectfully request the Examiner to enter the following Preliminary Amendment.

**AMENDMENT**

**In the Specification:**

At page 1, line 3, the RELATED APPLICATIONS section is amended to read as follows:

"This application is a continuation of copending application serial number 09/516,390, filed 1 March 2000, which is a continuation-in-part of application serial number 09/250,898 filed 16 February 1999, now abandoned, which is a non-provisional application of provisional application serial number 60/074,847, filed 17 February 1998".

**In the Claims:**

Claims 1 and 2 are cancelled.

New claims 3 through 8 are added as follows:

3. A transgenic mouse whose somatic and germ cells comprise a disruption in an endogenous H2-Oa gene, wherein disruption is generated by targeted replacement with a non-functional H2-Oa gene, and wherein said disruption results in said mouse having an increase in the amount of serum IgG1 at 10 months of age as compared to wild-type H2-Oa mice.
4. The mouse of claim 3, wherein said mouse is fertile and transmits the non-functional H2-Oa gene to its offspring.
5. The mouse of claim 3, wherein the non-functional H2-Oa gene has been introduced into an ancestor of the mouse at an embryonic stage by microinjection of altered embryonic stem cells into mouse blastocysts.
6. A method for producing a transgenic mouse whose somatic and germ cells comprise a disruption in an endogenous H2-Oa gene, wherein said disruption is generated by targeted replacement with a non-functional H2-Oa gene, said method comprising:
  - a) introducing a H2-Oa gene targeting construct comprising a selectable marker sequence into a mouse embryonic stem cell;
  - b) introducing said mouse embryonic stem cell into a mouse blastocyst;
  - c) transplanting said blastocyst into a recipient mouse;
  - d) allowing said blastocyst to develop to term;
  - e) identifying a transgenic mouse whose genome comprises a disruption of an endogenous H2-Oa gene in at least one allele; and

- f) breeding the mouse of step (e) to obtain a transgenic mouse whose genome comprises a homozygous disruption of the endogenous H2-Oa gene,  
wherein said disruption results in said mouse having an increase in the amount of serum IgG1 by ten months of age as compared to wild-type H2-Oa mice.
7. The method of claim 6 wherein the introducing of step (a) is by electroporation or microinjection.
8. An isolated cell line derived from the transgenic mouse of claim 3.

Respectfully submitted,

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DATE: 28 February 2002

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

At page 1, line 3, the RELATED APPLICATIONS section is amended to read as follows:

~~"This application is a continuation in part of application of co-pending application serial number 09/250,898, filed 16 February 1999, which is a non-provisional application of provisional application serial number 06/074,847, filed 17 February 1998, abandoned~~ This application is a continuation of copending application serial number 09/516,390, filed 1 March 2000, which is a continuation-in-part of application serial number 09/250,898 filed 16 February 1999, now abandoned, which is a non-provisional application of provisional application serial number 60/074,847, filed 17 February 1998".

In the Claims:

Claims 1 and 2 are cancelled.

New claims 3 through 8 are added as follows:

3. A transgenic mouse whose somatic and germ cells comprise a disruption in an endogenous H2-Oa gene, wherein disruption is generated by targeted replacement with a non-functional H2-Oa gene, and wherein said disruption results in said mouse having an increase in the amount of serum IgG1 at 10 months of age as compared to wild-type H2-Oa mice.
4. The mouse of claim 3, wherein said mouse is fertile and transmits the non-functional H2-Oa gene to its offspring.

5. The mouse of claim 3, wherein the non-functional H2-Oa gene has been introduced into an ancestor of the mouse at an embryonic stage by microinjection of altered embryonic stem cells into mouse blastocysts.
6. A method for producing a transgenic mouse whose somatic and germ cells comprise a disruption in an endogenous H2-Oa gene, wherein said disruption is generated by targeted replacement with a non-functional H2-Oa gene, said method comprising:
  - a) introducing a H2-Oa gene targeting construct comprising a selectable marker sequence into a mouse embryonic stem cell;
  - b) introducing said mouse embryonic stem cell into a mouse blastocyst;
  - c) transplanting said blastocyst into a recipient mouse;
  - d) allowing said blastocyst to develop to term;
  - e) identifying a transgenic mouse whose genome comprises a disruption of an endogenous H2-Oa gene in at least one allele; and
  - f) breeding the mouse of step (e) to obtain a transgenic mouse whose genome comprises a homozygous disruption of the endogenous H2-Oa gene,wherein said disruption results in said mouse having an increase in the amount of serum IgG1 by ten months of age as compared to wild-type H2-Oa mice.
7. The method of claim 6 wherein the introducing of step (a) is by electroporation or microinjection.
8. An isolated cell line derived from the transgenic mouse of claim 3.